Remarks

I. Status of the Application and Claims

As originally filed, the present application had a total of 10 claims. In previous prosecution, claims 1-10 were cancelled and new claims 11-27 were introduced. In the present response, claim 12 has been cancelled. Thus, the claims now pending are 11, and 13-27.

II. The Amendments

The specification was amended to change the title in accordance with the suggestion made by the Examiner on page 2 of the present Office Action and to move the Description of the Drawings to a place in the application immediately before the Detailed Description of the Invention.

Claims were amended to correct minor errors in the text that were pointed out in the Office Action, clarify subject matter claimed, correct typographical errors and improve readability. In addition, the limitations originally appearing in claim 12 have now been incorporated into claim 11. None of the amendments made herein add new matter to the application, and their entry is therefore respectfully requested.

III. Objections to Claims

On page 5 of the Office Action, the Examiner objects to claim 17. In part, the objection is made because the Examiner indicates that the genes *pntA* and *pntB* should be in separate paragraphs of the claim. However, Applicant submits that the intention is that *both pntA* and *pntB* be modified together, *i.e.*, neither should be the sole gene altered. This has been emphasized by slightly rewording the text to indicate that both genes must together be altered.

In addition, the Examiner objects to paragraphs y, z, yy and zz, because the article "a" is used when, in fact, the proper article would be "an." Applicant has amended claims to correct this error.

The Rejections

A. Response to Rejections in Item 9

On page 5 of the Office Action, in item 9, the Examiner rejects claims 11-27 as being indefinite because the term "modified" is unclear. In particular, the Examiner indicates that it is unclear whether the term refers to bacteria that have been modified by having their *yjgF* gene inactivated or bacteria that underwent some other type of modification. In fact, it is the former that was intended. However, to eliminate any confusion, Applicant has eliminated the term "modified" from claim 17 and has incorporated other language that should help to clarify the claimed subject matter.

B. Response to Rejection in Item 10

In item 10, the Examiner rejects claims 11 and 14-27 under 35 U.S.C. § 112, second paragraph as being indefinite allegedly because the term "*yjgF*" is not properly defined. In response, Applicant has noted that claim 12 was not included in this rejection and has amended claim 11 to incorporate the limitations of claim 12. In light of this change, Applicant respectfully submits that the Examiner's rejection has been overcome.

C. Response to Rejections in Item 11

In item 11, the Examiner rejects claims 17 and 18 under 35 U.S.C. § 112, second paragraph because it is allegedly unclear what genes are required to be over-expressed or inactivated by the claim limitations.

Applicant respectfully traverses this rejection.

Claim terms must be interpreted in light of the specification and each of the genes that is recited in claims 17 and 18 is described on pages 14-18 of the specification. In each case, a reference is provided which helps to define the gene and each of these references (with the exception of U.S. patent references) was submitted to the Examiner by Applicant along with the Information Disclosure Statement filed on November 18, 2004. Applicant respectfully submits that when the terms used in claims are properly interpreted in light of the specification, each gene recited is unambiguously identified in terms of its structure.

One thing that should be pointed out, however, both with respect to the genes recited within the body of claims as well as with regard to the "*E. coli yjgF* gene," is that, according to United States patent law, claims cover the sequences expressly recited and, under the doctrine of equivalents, other sequences that do not differ substantially from the exact sequences recited. It is not Applicant's intention to in any way compromise the scope of claims as interpreted under the doctrine of equivalents.

D. Response to Rejections in Item 12

In item 12, claim 17 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite because the term "a *thrA*" gene coding for aspartate kinase/homoserine dehydrogenase is allegedly confusing. The Examiner states that the two enzymes have different activities. In response, Applicant respectfully submits that the claim only refers to a single enzyme which is unusual in that it actually has two active sites and, as a result, does, in fact, have two activities. Claim 17 has been revised to try to make this more clear. The *thrA* gene is identified in the specification and a reference is cited (U.S. 4,278,765) that helps to define this gene and which was included in Applicant's Information Disclosure Statement filed on November 18, 2004 as document A1.

E. Response to Rejections in Item 13

In item 13 on page 7 of the Office Action, the Examiner rejects claim 17 under 35 U.S.C. § 112, second paragraph based upon the allegation that the phrases "a *pntA* and *pntB* gene coding for the subunits of pyridine transhydrogenase;" "a ahpC encoding the small subunit of alkyl hydroperoxide reductase;" and "a ahpF gene encoding the large subunit of alkyl hydroperoxide reductase" are unclear. The Examiner argues that the claim does not say how many subunits various enzymes have or what constitutes a "small" and "large" subunit.

In response, Applicant submits that the relevant issue with respect to 35 U.S.C. § 112, second paragraph is whether the subject matter recited in the claim, *i.e.*, specific genes, have been clearly defined in the specification. For each of the paragraphs in claim 17, individual genes are recited and a reference for the gene is provided in the specification on either page 14 or page 15. In the case of the *pntA* and *pntB* genes, a reference providing additional information (*Eur. J. Biochem. 158*:647-653 (1986)) is cited and was submitted in Applicant's

Information Disclosure Statement as document C7. A reference for the other two genes referred to in item 13 (WO 03/004663) was submitted as document B13. Upon having adequately defined each of the genes recited, Applicant's obligations under § 112, second paragraph have been fulfilled. There is no obligation to provide additional information concerning the number of subunits in the gene product or the structure of subunits.

F. Response to Rejections in Item 14

In item 14, the Examiner rejects claim 24 under 35 U.S.C. § 112, second paragraph as being indefinite based upon the allegation that the term "maximum amount" is unclear. In particular, the Examiner argues that it is not clear how one would tell when a maximum amount of L-amino acid has been produced in a fermentation procedure.

Applicant respectfully traverses this rejection.

The determination of the time when the concentration of a standard product, such as an amino acid, has reached a maximum in a fermentation is a routine matter in the art and requires nothing more than taking samples from the fermentation medium at different periods of time and analyzing them to determine the amount of amino acid present. An example generally showing this is provided in the specification in Example 4, pages 25 and 26, in which the amount of L-threonine produced after a period of fermentation is determined by amino acid analysis. Amino acid analyzers have long been used in the art and are capable of quantitating the amount of essentially any common amino acid produced in a procedure. Obviously, if a facility running a fermentation has carried out the same procedure a large number of times they could, if desire, simply wait a particular interval and collect product at that point. However, Applicant believes that, at least in large scale operations, sampling and amino acid quantitation using an amino acid analyzer or some similar procedure is standard practice. One of skill in the art would certainly not have trouble recognizing how to determine when to end a fermentation procedure, *i.e.*, when production is at a maximum, or what is meant in referring to "a maximum amount" of amino acid produced.

G. Response to Rejections in Item 15

In item 15, the Examiner rejects claims 11 and 14-27 based upon the written description requirement of 35 U.S.C. § 112, first paragraph. The main objection that has been made is that claim 11 defines the *yjgF* open reading frame solely by name and without any functional or structural limitations.

In response, Applicant has noted that claim 12 is not included in the rejection and has read the limitations of claim 12 into claim 11. It is therefore respectfully submitted that the Examiner's rejection has been overcome.

H. Response to Rejections in Item 16

In item 16, the Examiner rejects claims 17 and 18 based upon the allegation that a large variety of genes recited in these claims have not been adequately defined in the specification.

Applicant respectfully traverses this rejection.

For reasons that are unclear, the Examiner appears to have only recited a portion of the elements as they are actually present in the claim. For example, the Examiner refers to a "protein imparting homoserine resistance" when claim 17 actually refers to "the *Escherichia coli rhtB* gene coding for a protein imparting homoserine resistance." Taking portions of a definition out of context in this manner does not accurately reflect what the claim recites. In every case, a single gene is recited and, in most instances, the function of the gene is also mentioned.

Overall, the Examiner recites 29 elements in item 16 of the Office Action and consistently misstates the claim definition provided for every element. The recitation listed as (2) is typical. In this the Examiner alleges that claim 17 recites a gene "for a protein imparting threonine resistance" when, in fact, the claim actually recites "the *Escherichia coli rhtC* gene coding for a protein imparting threonine resistance." Applicant again submits that for every element recited in claims 17 and 18 a specific gene is recited and, in addition, the specification defines this gene and provides a reference which has been submitted by

Applicant to eliminate any confusion. Specific support for each of the genes objected to by the Examiner is as follows:

(1) Protein imparting homoserine resistance: (actually the *E. coli rhtB* gene) see EP 0 994 190; reference B36 in Applicant's Information Disclosure Statement.

(2) Protein imparting threonine resistance: (actually recited as the *E. coli rhtC* gene) see EP 1 013 765; reference B37 in Applicant's Information Disclosure Statement.

(3) Threonine export carrier protein: (actually recited in the claim as *C. glutamicum thrE* gene) see WO 01/92545; reference B4 in Applicant's Information Disclosure Statement.

(4) DNA-binding protein HLP-II: (actually recited as the hns gene) see WO 03/004671; reference B18 in Applicant's Information Disclosure Statement.

(5) Enzyme I of the phosphotransferase system: (actually recited in the claim as the ptsI gene) see WO 03/004674; reference B19 in Applicant's Information Disclosure Statement.

(6) Glucose-specific IIA component: (actually referred to as the crr gene) see WO 03/004674; reference B19 in Applicant's Information Disclosure Statement.

(7) Glucose-specific IIBC component: (actually recited in the claim as the ptsG gene) see WO 03/004670; reference B17 in Applicant's Information Disclosure Statement.

(8) Regulator of the leucine regulon: (actually recited in the claim as the lrp gene) see WO 03/004665; reference B15 in Applicant's Information Disclosure Statement.

(9) Csr: (actually recited in the claim as the csrA gene) see *J. Bacteriol. 175*:4744-4755 (1993); reference C44 in Applicant's Information Disclosure Statement

(10) regulator of fad regulon: (actually referred to in the claim as the fadR gene) see *Nucl. Ac. Res. 16*:7995-8009 (1988); reference C10 in Applicant's Information Disclosure Statement.

(11) Regulator of the central intermediate metabolism: (actually recited in the claim as the iclR gene) see *J. Bacteriol. 172*:2642-2649 (1996); reference C54 in Applicant's Information Disclosure Statement.

(12) 10 KD chaperone: (actually recited in the claim as the mopB gene) see WO 03/004669; reference B16 in Applicant's Information Disclosure Statement.

(13) Regulator of the cys regulon: (actually recited in the claim as the cysB gene) see WO 03/006666; reference B20 in Applicant's Information Disclosure Statement.

(14) PhoB: (actually recited in claim 17 as the phoB gene) see WO 03/008606; reference B24 in Applicant's Information Disclosure Statement.

(15) Sensor protein of the pho regulon: (actually recited in the claim as the phoR gene) see WO 03/008606; reference B24 in Applicant's Information Disclosure Statement.

(16) Protein E: (actually recited in the claim as the phoE gene) see WO 03/008606; reference B24 in Applicant's Information Disclosure Statement.

(17) Periplasmic binding protein of maltose transport: (actually recited in the claim as the malE gene) see WO 03/008605; reference B23 in Applicant's Information Disclosure Statement.

(18) Protein with anti-sigmaE activity: (actually recited in the claim as the rseA gene) see WO 03/008612; reference B29 in Applicant's Information Disclosure Statement.

(19) Global regulator of the sigmaE factor: (actually recited in the claim as the rseC gene) see WO 03/008612; reference B29 in Applicant's Information Disclosure Statement.

(20) Periplasmic protein with a chaperonin-like function: (actually recited in the claim as the hdeA gene) see *J. Bacteriol. 175*:7747-7748 (1993); reference C70 in Applicant's Information Disclosure Statement.

(21) Periplasmic protein with chaperonin-like function: (this appears to be the same element referred to previously by the Examiner as element (20).

(22) Periplasmic galactose-binding transport protein: (actually recited in the claim as the mglB gene) see *Mol. Gen. Genet. 229*:453-459 (1991); reference C18 in Applicant's Information Disclosure Statement.

(23) Iron storage homoprotein: (actually recited in the claim as the bfr gene) see *J. Bacteriol. 171*:3940-3947 (1989); reference C1 in Applicant's Information Disclosure Statement.

(24) Regulator of sigmaE factor activity: (actually recited in claim 17 as the rseB gene) see *Mol. Microbiol. 24*:355-371 (1997); reference C32 in Applicant's Information Disclosure Statement.

(25) *yifA*: (actually referred to in claim 18 as the open reading frame *yifA* of *E. coli*) see WO 02/29080; reference B6 in Applicant's Information Disclosure Statement.

(26) *ytfP*: (actually referred to in claim 18 as the open reading frame *ytfP* of *E. coli*) see WO 02/29080; reference B6 in Applicant's Information Disclosure Statement.

(27) DgsA: (actually referred to in claim 18 as the *dgsA* gene) see WO 02/36797; reference B7 in Applicant's Information Disclosure Statement.

(28) Fructose repressor: (actually referred to in claim 18 as the *E. coli fruR* gene) see WO 02/081698; reference B9 in Applicant's Information Disclosure Statement.

(29) Sigma^{38} factor: (actually referred to in claim 18 as the *rpoF* gene) see WO 01/05939; reference B3 in Applicant's Information Disclosure Statement.

When each of the elements recited by the Examiner is actually read in context and properly, a single gene is recited and, as set forth in the list above, the specification provides a reference in each case that helps in defining the gene. Each of these references has already been submitted to the Examiner. Applicant therefore respectfully submits that the allegation that the written description requirement for these elements has not been met is incorrect.

I. Response to Rejections in Item 17

In item 17 on pages 12-15 of the Office Action, the Examiner rejects claims 11 and 14-27 under the enablement requirement of 35 U.S.C. § 112, first paragraph. As with the written description rejection that was made earlier, the Examiner has not included claim 12 in the rejection. Since Applicant has read in all of the limitations of claim 12 into claim 11, it is respectfully submitted that the Examiner's rejection has been obviated.

Conclusion

In light of the amendments and discussion above, Applicant believes that all of the Examiner's rejections have been overcome. It is therefore respectfully requested that these rejections be withdrawn and that the claims now pending be allowed. Early notice to this effect is earnestly solicited.

If, in the opinion of the Examiner, a phone call may help to expedite the prosecution of this application, the Examiner is invited to call Applicant's undersigned attorney at (202) 419-7013.

Respectfully submitted,

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